

Industry Horizons: Chemistry & Life Sciences Office

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Current Portfolio of Technology Areas

- Materials Technologies
 - advanced materials
 - materials processing
 - materials surface dynamics
 - integration w/ knowledge tools
- Chemistry & Process Science
 - reaction design & processing
 - separations/membranes
 - high-throughput screening & synthesis methods

- Life Sciences
 - DNA analysis
 - tissue engineering
 - medical devices
 - agricultural biotech





Project Highlights: Materials Technologies

Project Impact Areas:

- **Engineered Surfaces** -- methods to enable reliability, predictability & extended lifetimes in harsh environments
- Advanced Composites -- methods to enable structural applications with enhanced performance
- Powder Processing -- methods to enable microstructure control needed for high-performance components
- Innovative Forming -- techniques to minimize post-fab machining and reduce development cycle time
- Manufacturing Methods for Materials -- methods to enable process agility or condition-based monitoring





Automotive Composites Structures: High Volume Manufacturing Technology

Goal: Development of an enabling composites manufacturing technology to speed creation of lighter-weight, fuel efficient and corrosion-free vehicles.

Key Technical Challenge: Development and integration of robust high-volume manufacturing processes for large structural components such as pickup beds.

Core Innovation: New powder preform, injection molding and assembly processes enabled cost-effective production of large, lightweight complex parts.



General Motors,

Daimler Chrysler, Ford Motor Co.

Start/End: 03/95 to 02/97

ATP funds: \$3,273 K

University of Detroit Mercy

10 small business subcontractors





Development of TERFENOL-D High-Powered Ultrasonic Transducer for Use in Sonochemistry

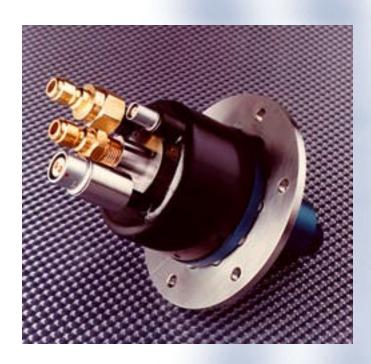
Goal: Increase power output of an ultrasonic motor by a factor of 4-10X enabling sonochemistry applications for:

- **enhanced** oil recovery
- **a**de-vulcanization of rubber
- **increased seed germination yield**

Key Technical Challenge: Current materials cannot handle extreme forces, heat or mechanical instability generated by high ultrasonic power and magnetic hysteresis.

Core Innovations:

- **Materials design to control microstructure**, tailoring mechanical, thermal, magnetic properties
- **Non-linear modeling and design stabilizes thermal** and mechanical loading
- **Feedback control for load change damage** prevention
- Invention of new power amplification



ETREMA Products. Inc.

Start/End: 10/97 to 06/00

ATP funds: \$699 K

Iowa State Univ. Univ of Maryland

Univ. of Calif Berkeley



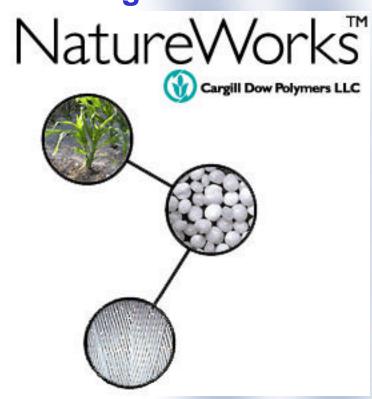


Development of Improved Functional Properties in Renewable-Resource-Based, Biodegradable Plastics

Goal: Improve the properties of a potentially-inexpensive, biodegradable plastic (polylactide or PLA) which is produced from corn sugar. Replacing petroleum-based plastics with PLA could help the economy become more environmentally sustainable.

Key Technical Challenge: Low heat-resistance is the major shortfall of any PLA that has been produced in the past. Without a technology for increasing its melting point and heat-transition temperature, PLA will not be able to compete against existing, commercially-successful petroleum-based plastics.

<u>Core Innovation</u>: Crystallinity is a key variable for increasing heat-resistance in PLA. The project resulted in an understanding of and methods for crystallinity control in PLA over a wide range of processing conditions.



Cargill Dow Polymers, LLC

Start: 2/95 to 1/98 ATP funds: \$1,994 K

5 Universities + 2 small mfg-ers





Project Highlights: Chemistry & Process Science

Cost-effective design methods for environmentally benign routes to materials, chemical building blocks, industrial gases, drugs, food processing etc.

Project Impact Areas:

- Reaction Design -- active site design tools and methods to speed development cycle of catalytic and biocatalytic processes and enable whole new chemistries
- Process Science -- methods to integrate advanced reaction design techniques and product recovery technologies into cost-effective processes
- High Throughput Methods -- combinatorial methods for material design, reaction engineering, and processing techniques



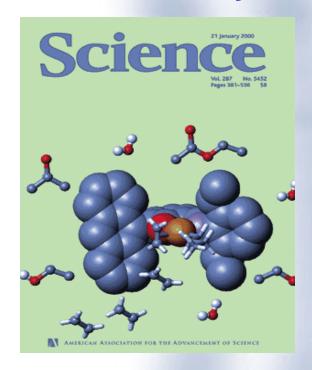


Polar Tolerant Organometallic Catalytic Technology for Functionalized Linear Polyolefins

Goal: Design methods for a new family of polymer catalysts for producing chlorine-free plastic film with superior processing stability, oxygen barrier rating, and biodegradability, as for food packaging.

Key Technical Challenge: Polymerization systems are typically unable to tolerate polar heteroatoms such as oxygen or nitrogen, thus requiring high-purity starting materials and activating cocatalysts.

Core Innovation: This new nickel-based catalyst system overcomes these limitations. New modular ligand design methods afford unique control over polymer properties and structure.



Cryovac, Inc. North America, Sealed Air Corp. (formerly W.R. Grace)

Start/End: 10/95 to 10/98

ATP funds: \$2,000 K

California Inst. of Technology



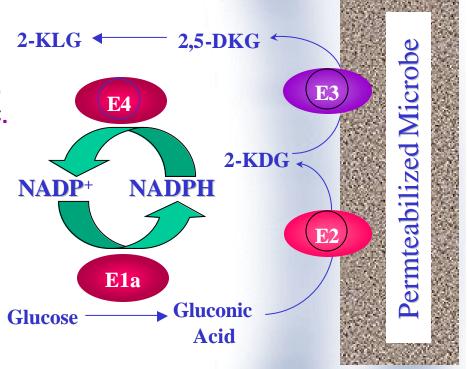


Continuous Biocatalytic Systems for the Production of Chemicals from Renewable Resources

Goal: Develop a new, lower-cost, single-step, environmentally-sustainable, biocatalytic technology that can replace the multi-step, chemical processes which are currently used to produce important chemicals such as Vitamin C.

Key Technical Challenge: Any process must perform reactions which are normally incompatible (oxidation and reduction) in the same 'micro-reactor' (e.g., microbial cell).

Core Innovations: Recruit enzymes from different microorganisms to engineer a single organism which can do the entire conversion. Engineer key enzymes onto a microbial 'scaffold' to increase enzyme life and substrate turnover through the pathway.



Genencor, Eastman Chemical, Electrosynthesis, Microgenomics and Argonne National Lab.

Start: 9/95 to 9/00

ATP funds: \$15,623 K

Rutgers University & Univ. of Tennessee





Project Highlights: Life Sciences

DNA Analysis & Gene Expression

Provide low cost DNA analysis for broad application: health, agriculture, food technologies, bioprocessing

Project Impact Areas:

- **complete systems --** one chip or cartridge systems
- hybridization arrays -- parallel analysis w/DNA probes
- microfluidic devices -- moving fluids on chips
- electrophoresis -- DNA sequencing
- mass spectrometry -- genotyping, products of sequencing reactions
- enzymology and chemistry -- reagents for sequencing and amplification of DNA





Miniature Integrated Nucleic AciD (MINDTM) Diagnostic Development

Goal: Develop <u>miniaturized integrated</u> DNA diagnostic system for clinical applications.

Key Technical Challenge: Integration of all the processes in DNA analysis into a single chip/cartridge format to enable, with database technologies, user friendly DNA diagnostic systems for clinical use.

Core Innovation: Integrate photolithography and DNA probe synthesis methods to fabricate dense DNA arrays. Fabrication methods of chips for electrophoresis analysis (96 lanes) comparable in resolution to conventional method. Integrate all steps from sample preparation to DNA analysis (hybridization or electrophoresis) onto a single chip/cartridge.



Affymetrix, Amersham Pharmacia Biotech (Molecular Dynamics), Molecular Applications Group

Start/End: 02/95 to 01/00

ATP funds: \$31,500 K

6 Universities, 5 small business





- 1) Development of a Generic Technology for the Targeted Detection of Cleavage of DNA and RNA
- 2) Simple, Generic, Low Cost Genetic Based Tools for Disease Detection, Monitoring and Intervention

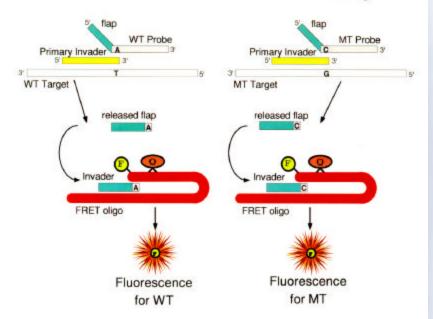
Goal: 1) Development of Cleavase™ enzymes for cleaving of doubly stranded DNA at a variety of mismatch sites. 2) Development of isothermal based DNA amplification and its application to inexpensive diagnostics.

Key Technical Challenge: Integration of the two unique methodologies into a simple format for rapid inexpensive DNA diagnostics.

Core Innovation: 1) Development of a robust cleavase enzymology with a low cost production method.

2) Development of a robust isothermal DNA amplification technology.

Schematic of the Invader™ Assay



Third Wave Technologies Start/End: 01/95 to 12/96

10/97 to 09/99

ATP funds: \$2,000 K each

University of Wisconsin





Project Highlights: Life Sciences (cont'd)

Tissue Engineering

Provides synthetic bioequivalent biocompatible organ replacements.

Project Impact Areas:

- xenotransplantation -- organs, tissues and cells
- scaffolding -- cartilage, bone, vascular systems
- human cell culture -- liver, blood, pancreas
- encapsulation -- cells producing therapeutics (insulin)
- animals as bioreactors -- vaccines, specialty proteins





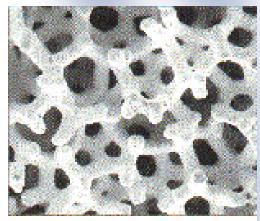
Ex vivo Production of Universal Red Blood cells and Platelets in a Biocompatible 3-D Tissue Scaffold

Goal: Develop an alternative source of red blood cells through production of universal red blood cells and platelets in a biocompatible, 3-D scaffold.

Key Technical Challenge:

- **The Interview of the Example 1** Hematopoietic stem cell survival in cytokine free static Cellfoam cultures.
- Four month survival of HSCs in the absence of cytokines.
- **©** Culture, harvest, and analyze isolated cells.

Core Innovation: Utilize the Cellfoam platform to support continuous, steady state perfusion of cultured cells to demonstrate the ability to expand and maintain multipotency of HSC ex vivo for extended periods.



Cellfoam is a unique, three-dimensional cell growth matrix

Cytomatrix, Inc.

Start/End: 01/98 to 12/00

ATP funds: \$1,319 K





Universal Donor Organs for Transplantation

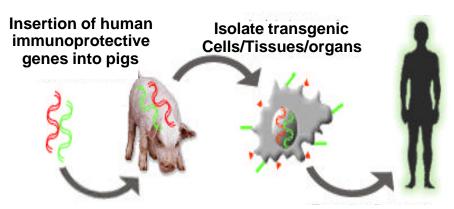
Transplanted
Cells/Tissues/Organs with
inserted human genes
resist rejection

Goal: Develop transgenic pigs as a universal source of donor organs for transplantation that incorporate human genes to eliminate hyperacute rejection (HAR).

Key Technical Challenge:

Generate transgenic founder pigs with high levels of expression of protective factors. Evaluate natural antibody reactivity and complement regulatory function in a pig to primate model transplant system.

Core Innovation: Attempt to eliminate HAR by genetically engineering pig tissue to express a human inhibitor (CD59), and a human blood group enzyme (H-transferase).



Transplant Protected Cells/Tissues/Organs into Patient

Alexion Pharmaceuticals, Inc.

Start/End Dates: 9/95 - 9/99

ATP funding \$2,000 K

Tufts University Oregon Health Sciences Univ.



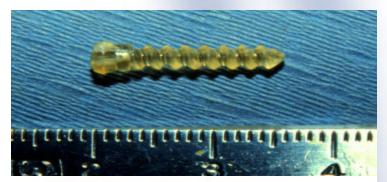


Structurally New Biopolymers Derived from Alpha-L-Amino Acids

Goal: Develop new class of bioabsorbable polymers based on tyrosine for use as pins and screws in the repair of fractured bones as a replacement for metal and other non-resorbable materials currently used.

Key Technical Challenge: Synthesis and characterization of bioabsorbable tyrosine polycarbonates. Studies to determine key properties: mechanical, resorption and biocompatibility. No harmful byproducts can be released upon degradation.

Core Innovation: Successful development of a process to produce commercial quantities of tyrosine-based polymers at \$3-5/gm





New Bone Bridging the Implant

Integra Life Sciences Corp.

Start/End: 01/94 to 04/97

ATP funds: \$2,000 K

Rutgers University

Hospital for Joint Diseases





Industry Horizons: Materials Technologies

- Increasing complexity of materials and manufacturing at smaller dimensions
- Incorporating knowledge of biological systems into material design methods
 bio-active, bio-mimetic, biodegradable, self-assembly
- Integrating high-throughput, lifetime simulation, and novel CAD techniques into material and process design methods



Industry Horizons: ADVANCED TECHNOLOGY PROGRAM Chemistry & Processing Science

- Integrating high-throughput methods and computational tools
 - materials design & discovery
 - process development: micro reactors
- Bioprocessing for chemicals & materials
- Green chemistry
- Reducing process complexity
 - novel reactor concepts to reduce number of operations or enhance process agility
 - smart materials for membranes





Industry Horizons: Life Sciences

- Gene Therapy: placing genes in living systems which express specific therapeutic proteins
- <u>Stem Cells:</u> controlling the maturation & development of a functional cell from its uncommitted form for therapeutic transplantation.
- Structural Biology & Proteomics: methods for using genomic & protein structure data (eg, function & expression) for complex biosystems to design diagnostics & therapeutics
- <u>Vaccines:</u> applying molecular biology design methods to trigger immunity
- Biosensors: in vivo biocompatible sensors
- Nanotechnology: uses in tissue engineering, biosensors and DNA diagnostics



THE NEW ERA OF REGENERATIVE MEDICINE

Dozens of biotech companies and university labs are developing ways to replace or regenerate failed body parts. Here are a few of the projects:



BONE

Bone-growth factors or stem cells are inserted into a porous material cut to a specific shape, creating new jaws or limbs. A product that creates shinbones is in clinical trials.

COMPANIES: Creative Biomolecules, Orquest, Sulzer Orthopedics Biologics, Genetics Institute, Osiris Therapeutics, Regeneron.



SKIN

Organogenesis' Apligraf, a human-skin equivalent, is the first engineered body part to win FDA approval, initially for leg

ulcers. Other skins are in the works for foot ulcers and burns.

COMPANIES: Organogenesis,
Ad-vanced Tissue Sciences,
Integra LifeSciences, LifeCell, Ortec International.



PANCREAS

insulin-manufacturing cells are harvested from pigs, encapsulated in membranes, and injected into the abdomen. The method has been tested in animals and could be in human trials in two years.

COMPANIES: BioHybrid Technologies, Neocrin, Circe Riomedical



HEART VALVES, ARTERIES, AND VEINS

A 10-year initiative to build a heart has just started. Genetically engineered proteins have been successfully used to regrow blood vessels.

COMPANIES: Organogenesis, Advanced Tissue Sciences, Genetech, LifeCell, Reprogenesis.

DATA: BUSINESS WEEK, DRUG & MARKET DEVELOPMENT REPORTS



SALIVA

Proteins called aquaporins that allow cells to secrete water are used to recreate

saliva glands damaged by disease or radiation. Glands are also being engineered to secrete healing drugs. The technique has proven successful in mice.

COMPANIES: None yet.



URINARY

Cartilage cells are taken from the patient, packed into a tiny matrix, and injected into

the weakened ureter, where they bulk up the tissue walls to prevent urinary backup and incontinence. The method is in late-phase clinical trials.





BLADDER

Doctors at Children's Hospital in Boston have grown bladders from skin cells and implanted them in sheep.

They are about to try the same process on a patient

COMPANIES: Reprogenesis.



CARTILAGE

A product is already on the market that regrows knee cartilage. A chest has been grown for a boy and a human

ear on a mouse.

COMPANIES: Genzyme Tissue, Biomatrix, Integra LifeSciences, Advanced Tissue Sciences, ReGen Biologics, Osiris Therapeutics



TEETH

Enamel matrix proteins are used to fill cavities. It works in dogs; human trials are a few years away.

companies: Biora, Atrix Laboratories, Creative BioMolecules.



BREAST

In preclinical studies, several companies have been able to create a cosmetic nipple by

inserting a ball of cartilage. Researchers are now trying to grow a whole cosmetic breast.

COMPANIES: Reprogenesis, Integra LifeSciences.



LIVER

A spongy membrane is built up and then seeded with liver cells. Organs the size of a dime

have been grown, but a full-size liver could take 10 years due to its complexity.

COMPANIES: Advanced Tissue Sciences, Human Organ Sciences, Organogenesis.



SPINAL

Scientists are in-vestigating nerve-growth factors, inject-

ing them at the site of damage to encourage regeneration or seeding them along biodegradable filaments and implanting them. Rats have been made to walk again.

COMPANIES: Acorda, Regeneron, CytoTherapeutics, Guilford Pharmaceuticals.



Action Plans: Supporting Industry's Vision

- Clarify with industry input how world-class high risk engineering and innovative systems integration can meet ATP criteria
- Increase collaboration with mission agencies to enhance industry understanding of ATP niche in biotechnology, materials science, and chemistry
- Participate in cross-technology teaming w/NIST labs and industry to refine NIST competencies that support tissue engineering and combinatorial methods.
- Expand educational outreach to industry concerning protection of human and animal subjects in research.

